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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,816	07/30/2001	Francesco Mehlem	APV31199	9641

7590 05/30/2003

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EXAMINER

TELLER, ROY R

ART UNIT PAPER NUMBER

1654

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/831,816

Applicant(s)

MEHLEM ET AL.

Examiner

Roy Teller

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 July 2001.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.                      6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This office action is in response to Paper No: 5, received 7/30/01, in which claims 1-7 were amended and new claims 8-14 were added.

Claims 1-14 will be examined.

#### ***Information Disclosure Statement***

The information disclosure statement filed 6/20/01 (Paper No: 2) is acknowledged. A signed copy is attached hereto.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Barbieri, USPN 3,814,746, in view of Mehlem, WO 99/02177.

The instant invention is drawn to a method of producing at least one member of the group consisting of L-prolyl-L-m-sarcosyl-L-p-fluorophenylalanine, a lower alkyl ester thereof and acid addition salts thereof.

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De Barbieri teaches the synthesis of peptide moiety, compound 158/4, L-prolyl-m-(ci-(2-chloroethyl)-amino)-L-phenylalanyl-p-fluoro-L-phenylalanine ethyl ester hydrochloride, see column 8, line 15- column 9, line 2. De Barbieri discloses adding to a chloroform solution containing 40g. of m-(di(2-chloroethyl)-amino)-L-phenylalanine ethyl ester were added 29.9 g. of N-carbobenzoxyl-L-proline, dissolved in 60ml. of chloroform, see column 8, lines 21-26. De Barbieri teaches carbobenzoxyl removal: 15g. of N-carbobenzoxyl-L-prolyl-m-(di(2-chloroethyl)-amino)-L-phenylalanyl-p-fluoro-L-phenylalanine ethyl ester were dissolved by heating in 10 volumes of 5% HCL in absolute ethyl alcohol, hydrogenated in the presence of about 2 g. of palladized charcoal to complete CO<sub>2</sub> elimination, see column 8, lines 64-69. De Barbieri discloses that tetracycline derivatives of synthetic peptides having m-di(2-chloroethyl)amino-phenyl-L-alanine linked through one or more peptide bonds to one or more specified amino acids, are effective in the treatment of tumors in man and other animals, see abstract. De Barbieri does not teach a method involving glacial acetic acid.

Mehlem teaches the synthesis of L-prolyl-L-m-sarcosyl-L-p-fluorophenylalanine ethyl ester hydrochloride, see page 4, line 16- page 10, line 14 (equivalent to pages 6- 11 of the instant specification). Mehlem discloses a mixture of N-carbobenzoxyl-L-prolyl-L-m-sarcosyl-L-p-fluorophenylalanine ethyl ester and 30 g. of palladium on 5% carbon suspended under a stream of nitrogen in 15 ml. of glacial acetic acid and under 1750 ml. of methanol, see page 9, lines 7-10 (equivalent to page 11, lines 1-4 of the instant specification).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added the methodology of Mehlem with the methodology of De Barbieri in order to enhance the composition that is effective in the treatment of tumors.

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***Conclusion***

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy Teller whose telephone number is (703) 305-4243. The examiner can normally be reached on Monday-Friday from 5:30 am to 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (703) 306-3220. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RT  
1654  
5/27/03  
RT

  
**BRENDA BRUMBACK**  
**SUPERVISORY PATENT EXAMINER**  
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